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1 **Title:** A multicentre development and evaluation of a dietetic referral score for nutritional
2 risk in sick infants

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27 **Short title:** A nutrition warning score for sick infants

28

29

30 **Clinical Trial registration:** <https://clinicaltrials.gov/ct2/show/NCT03323957>

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32

33 **Keywords:** malnutrition, infants, nutritional risk, nutrition screening tool

34

35 **Abbreviations:** iNEWS: infant nutrition early warning score

36

37

38 **Abstract**

39 **Background & Aims:** Unrecognized nutritional issues may delay recovery in hospitalized
40 infants. It has been proposed that nutritional risk screening should be performed at hospital
41 admission, but few tools include infants. The aim of this study was to develop and test a tool
42 to identify sick infants in need of dietetic input.

43 **Methods:** Hospitalised infants were recruited from hospitals in the United Kingdom (UK),
44 Greece and Iran. Weight, skinfold thickness and mid upper arm circumference (MUAC) were
45 measured, with detailed dietetic assessment in the UK and Greece. Simple screening
46 questions were used in the UK cohort to formulate a score (infant early nutrition warning
47 score-iNEWS) which was then validated in the Greek and Iranian groups.

48 **Results:** After dietetic assessment, 20 (9.6%) UK and 22 (22%) Greek infants were rated as
49 needing dietetic input. Underweight, poor weight gain/loss and reduced intake were all
50 independent predictors of perceived need for dietetic input in stepwise multivariate regression
51 analysis. The score based on these items (iNEWS), had 84% sensitivity, 91% specificity and
52 49% positive predictive value to predict need for dietetic input in the UK cohort. In the Greek
53 cohort this was 86%, 78% and 53% respectively. In all three countries, infants with high
54 iNEWS had significantly lower average skinfold thickness (between -1 to -1.8 SD, $p<0.0001$)
55 and MUAC (between -1.8 to -2 SD, $p<0.0001$) than those at low risk.

56 **Conclusions:** iNEWS, a simple nutritional risk tool, identifies most hospitalised infants who
57 need dietetic input.

58

59 **Word count:** 2,867

60 **Introduction**

61 It has been argued, that sick children in need of nutritional intervention often remain
62 undetected and untreated in clinical practice [1] and that a process of screening, assessment
63 and treatment of children at nutritional risk should be introduced in routine admission
64 procedures. As dieticians are usually a scarce resource, it has been proposed that nutritional
65 screening tools (NST) should be used by nursing staff or junior paediatricians to identify
66 children needing dietetic input [2].

67 Several NST have been developed for paediatric inpatients and have been compared
68 in different studies against various benchmarks of nutritional risk [3, 4]. As there is no gold
69 standard measurement of nutritional risk, the comparators used in most studies have either
70 been other NST [5] or anthropometry[6, 7]. This introduces circularity as low weight or BMI
71 often also forms part of the NST. As the real objective of a NST is to identify children who
72 require dietetic input, this should be the appropriate benchmark to use to assess screening
73 validity. Previous studies also rarely addressed the practical utility of NST which need to be
74 quick and simple and should identify cases that would otherwise be missed [8], while not
75 identifying too many false positives.

76 The highest proportion of sick children at nutritional risk is infants and neonates [9]
77 and their rapid growth means that NST designed for children are unlikely to be valid. Yet
78 there is only one NST which included any infants in its development and none which
79 includes infants aged under one month [4]. Hence, there is clearly a need to develop and test
80 a NST for this early age range.

81 The aim of this study was to develop and test a tool which will identify infants in need
82 of dietetic input, using data from three different international settings. Our detailed objectives
83 were:

- 84 1. Collect data on four clinical predictors of nutritional risk in hospitalised infants in the
85 UK and explore their ability to predict need for dietetic input.
- 86 2. Use these predictors to derive a weighted nutritional risk score and define the most
87 effective screening threshold.
- 88 3. Assess the screening validity of the nutritional risk score when applied to an
89 independent Greek cohort.
- 90 4. Test the score's discriminant validity using skinfold thickness and mid upper arm
91 circumference (MUAC), as independent proxies of nutritional risk in the UK, Greek
92 and Iranian datasets.

93

94 **Materials and Methods**

95 *Recruitment*

96 Convenience samples of inpatients were recruited from a variety of clinical specialties in
97 three tertiary children's hospitals: Glasgow, United Kingdom (UK), Athens, Greece and
98 Tabriz, Iran. Recruitment was carried out from January 5th 2011 to July 28th 2013. Infants
99 were eligible for recruitment if they were less than one year of age, admitted from home and
100 had been an inpatient for less than 48 hours. Patients from the short stay ward, oncology unit,
101 intensive care unit were not included and in Iran all children under four weeks old were
102 excluded, as in that setting many of these children had been admitted directly from other units
103 due to problems at birth. Most eligible admissions were studied, but apparently higher risk
104 infants were prioritised to ensure sufficient numbers of high risk cases.

105 Measurements of weight and length were collected according to the WHO standard
106 operational procedures and were converted into z-scores using the WHO international data
107 [5, 9]. For infants over 3 months old, the triceps and subscapular skinfolds were converted
108 into z-scores using the WHO standards, which are only available from the age of three
109 months. The average skinfold z-score was then calculated for the two skinfold sites and used
110 in subsequent analysis.

111 Comprehensive nutritional assessment was performed in the UK by three qualified
112 research dietitians/nutritionists and in Greece by the three hospital paediatric dietitians. The
113 assessment included measurements of weight and length, growth trajectory, dietary intake,
114 clinical and any available laboratory data. The dietitians then recorded whether they judged
115 that dietetic input would be justified or not. This outcome comprised the benchmark for the
116 development and validation study of the iNEWS, as it was considered to have direct clinical

117 relevance for routine practice. Data on patient demographics and disease characteristics were
118 retrieved from the medical notes and via caregiver interview.

119

120 *Development of the infant nutrition early warning score (iNEWS).*

121 The initial candidate components for the tool were based on the ESPEN recommendations for
122 nutritional screening [10]. The four '*a priori*' selected predictors were:

123 1. Weight below 9th centile or 2nd centile, indicating the current nutritional status of the
124 infant.

125 2. Health professional's concern about slow weight gain, as reported by the caregivers,
126 suggesting recent deterioration of nutritional status.

127 3. Reported decrease in usual dietary intake for more than 5 days, indicating increased
128 likelihood of future deterioration of nutritional status.

129 4. The impact of the admission condition (as judged by the assessor) on infant's nutritional
130 risk, suggesting increased future risk of deterioration in nutritional status.

131 At the early development stage each item was reported in Yes/No format, with no scoring
132 assigned to each of these nutritional risk predictors.

133 Using the UK dataset, these predictors were regressed against the outcome of the
134 comprehensive nutritional assessment (i.e. need for dietetic input), using binary logistic
135 regression analysis. The predictors which were statistically significant ($p < 0.05$) in univariate
136 analysis were introduced stepwise in a multivariate model, starting from the predictors which
137 explained the largest variation (i.e. highest coefficient of determination) in the outcome
138 variable. Non-significant predictors were removed from the model until a final model with
139 only significant predictors was concluded.

140 The β coefficients of each of the significant predictors in the final multivariate model
141 were then used as scores in the final prototype tool. The optimal overall iNEWS screening
142 threshold for referral for dietetic input was defined using Receivers Operating Curve (ROC)
143 analysis.

144

145 *Cross-validation in a second independent international cohort*

146 The iNEWS score was then cross-validated using the Greek cohort, where hospital dietetic
147 staff performed comprehensive nutritional assessment independently. The sensitivity,
148 specificity and positive and negative predictive values of iNEWS were calculated.
149 Assessment of diagnostic validity was not possible in Iran as hospital dietitians were not
150 available.

151

152 *Discriminant validity*

153 In all three international cohorts, the discriminant validity of iNEWS was tested using the
154 extent to which iNEWS distinguished between children with high and low body fat stores as
155 well as against MUAC measurements. The proportion of children with both BMI z-score and
156 mean skinfold thickness z-score < 2nd centile was calculated and grouped according to their
157 iNEWS screening outcome.

158 Statistical analysis was performed with MINITAB version 17 Ltd, UK and MedCalc
159 Statistical Software version 17.6 (MedCalc Software bvba, Ostend, Belgium).

160 *Sample size calculation*

161 Power calculation was performed for the assessment of discriminant validity of iNEWS.
162 Using the Altman nomogram, 70 subjects per group gave 80% power to detect a difference of
163 0.5 SD in skinfolds between any two groups.

164 *Ethical considerations*

165 The study was conducted in accordance with the guidelines outlined in the Declaration of
166 Helsinki and all procedures involving human subjects were approved by the West of Scotland
167 Research Ethics Committee, Glasgow, the Ethics Committee of the Paediatric Health
168 Research Centre in Tabriz University, Tabriz and the Ethics Committee of the General
169 Children's Hospital "Pan. & Aglaia Kyriakou" in Athens. Infants' parents provided written
170 consent. The study was registered under in www.clinicaltrials.gov (NCT03323957).

171 **Results**

172 *Subject characteristics*

173 In total, 499 infants [mean (SD), age; 0.41 (0.28) y, males, n=296 (59%)] were recruited from
174 all centres (Figure 1). Around half of the infants were admitted with medical infectious
175 diseases, with the highest proportion in Iran, while 16-25% were admitted for surgical
176 procedures (Table 1). Infants from Iran were significantly shorter than the other two cohorts
177 and mean weight and BMI z-scores were significantly lower in the Greek and Iranian
178 children than their Scottish counterparts (Table 1). Sixty four (13%), 120 (25%) and 130
179 (27%) of the infants were classified as short, underweight and thin respectively, with
180 significantly higher proportions observed in the Greek and Iranian groups (Table 1). There
181 were 307 children aged over 3 months with skinfold measurements for whom WHO
182 standards are available. 92 (30%) of these had a mean z-score measurement below -2 SD (2nd
183 centile). A significantly higher proportion of infants with suboptimal fat stores were seen in
184 Iran and Greece than in the UK (Table 1). In the UK and Greece, where comprehensive
185 dietary assessment was performed, 20 (9.6%) and 22 (22%) respectively, were rated as
186 needing dietetic input.

187 *Development of iNEWS*

188 In univariate logistic regression analysis, all four of the putative predictors were predictive of
189 need for dietetic input (validation outcome). In stepwise multivariate analysis, the effect of
190 the current medical condition on nutritional risk was not independently predictive, so it was
191 excluded from the final model (Table 2).

192 *Selection of optimal referral threshold and screening validity*

193 A weighted score was then developed using the β coefficients of the three remaining steps
194 (Table 2). Using ROC analysis, the optimal screening threshold of iNEWS was a total score
195 of greater than 3.9, with 84% sensitivity, 91% specificity, 49% positive predictive value
196 (PPV) and 98% negative predictive value (NPV) in the UK cohort. The screening validity of
197 iNEWS using other screening thresholds is presented in Table 3. Applying this score and
198 threshold to the Greek cohort produced a very similar sensitivity (86%), PPV (53%) and NPV
199 (95%), despite a slightly lower specificity 78% (Table 4). Collectively, 33 (16%) of the UK,
200 36 (36%) of the Greek and 83 (46%) of the Iranian infants had iNEWS > 3.9 and were thus
201 screened positive. The final iNEWS form is presented in Figure 2 in the format of a) a
202 numerical-based layout and b) a decision-tree based algorithm. A high resolution form and
203 quick reference guide on how to use iNEWS is presented as Online Supplementary Files.

204

205 *Analysis of misclassified cases*

206 Of the 69 screen positive infants in the Greek and the UK cohorts who also had dietetic
207 assessment, 34 (49%) were rated as not needing dietetic input. There was a trend for infants
208 with false positive screens to have a medical condition associated with increased nutritional
209 risk (63% vs 37%; $p=0.102$) and a shorter length of hospital stay (4 vs 5 days; $p=0.063$) than
210 the true positive cases of nutritional risk. Only six of the infants screened as low risk using
211 iNEWS were rated as needing dietetic input. No characteristic distinguished these children
212 from the true positive screens.

213

214 *Discriminant validity of iNEWS*

215 The skinfold thickness and MUAC z-score of patients classed at high nutritional risk were
216 one to two SD lower than those at low risk in each country (Table 4). Among the infants with
217 low average skinfold measurements (< 2nd centile), 29% (2/7) UK, 54% (14/26) Greek and
218 80% (47/59) of the Iranian infants had high risk iNEWS. From the 299 children with
219 measurements of both BMI and skinfolds, 66 (22%) had both of these below the 2nd centile
220 indicating children who were both thin and had depleted fat mass stores. In this group, 50%
221 (2/4) in the UK, 84% (38/45) in Iran and 76% (14/17) in Greece screened positive on iNEWS
222 (Figure 3). Infants with high iNEWS scores had a longer mean length of hospital stay than
223 those with low risk screens [iNEWS positive (SD) vs iNEWS negative (SD); 8.8 (8.3) vs 4.6
224 (3.9) days; $p < 0.0001$]. This effect was independent of country (data not displayed). The
225 discriminant validity of iNEWS against the WHO criteria of acute malnutrition is presented
226 in Table 4.

227

228 **Discussion**

229 Identification of hospitalized infants at high nutritional risk is clearly desirable, but at present
230 there is no consistent approach to this in routine hospital practice [11]. This study has shown
231 that a combination of the weight centile plus two screening questions identifies the majority
232 of children who need dietetic input, while only requiring a minority of infants to be further
233 assessed. Of the four elements studied, anthropometry was the strongest predictor, followed
234 by a history of poor weight gain/loss, while reduced dietary intake was the least predictive.

235 The predictive effect of the child's admission condition, which has been used in
236 previous scores [4, 12] proved not to be independently associated with the need of dietetic
237 input. Other NST use lists of diagnoses, but such lists can never be exhaustive and the
238 nutritional risk of patients with chronic illness can vary markedly during the course of their
239 disease [13]. The iNEWS therefore aimed to evaluate how the disease condition, at the point
240 of hospital admission, was likely to affect the infant's intake, requirements and losses.
241 Although in univariate analysis the patient's admission condition was predictive of valid
242 dietetic input, in multivariate analysis this effect lost statistical significance, suggesting that
243 most of this effect was explained by the other iNEWS components, including changes in
244 dietary intake and weight loss. By applying the current modelling methodology we were thus
245 able to remove a degree of predictor redundancy and simplify the tool further.

246 The binary nature of each iNEWS component offers a limited range of possible
247 alternative cut-offs and the optimal screening threshold was chosen with the aim of
248 optimising both sensitivity and specificity. Using the iNEWS cut-off of 3.9, defines all
249 infants below the WHO 2nd weight centile as high risk, as well as infants with slow weight
250 gain/loss who are below the 9th centile, or an infant of any weight with both slow weight gain
251 and reduced intake (Figure 2).

252 Very few children rated as needing dietetic input were missed by iNEWS screening
253 and no characteristic distinguished these cases from those correctly identified. In contrast, the
254 false positive screens were slightly more likely to suffer from a condition associated with
255 high nutritional risk. Although this was of only borderline statistical significance, this further
256 suggests that the underlying condition is not always usefully informative about nutritional
257 risk. These infants may have experienced a recent decrease in dietary intake and transient
258 weight loss, but were on the whole not at long-term nutritional risk. Although roughly half of
259 the children who screened positive proved not to be at real nutritional risk, this is an
260 acceptable false positive rate, which in a UK or Greek context would not represent
261 unmanageable referral rates.

262 The study aimed to oversample for high risk patients and thus did not recruit a fully
263 representative population, which in developed countries would mainly comprise low risk
264 cases [5]. In the Iranian sample nearly half the infants studied screened positive, but their
265 skinfold and MUAC results suggest that rates of actual malnutrition were truly high. Use of
266 iNEWS in this country could be expected to halve the number of children needing to be
267 referred for dietetic assessment.

268 If avoidance of false positive referrals was the priority, a higher cut-off of 4.2 could
269 be used instead, which would include infants with weight below 2nd centile if they also had
270 either slow weight gain or reduced intake, or infants below 9th with both slow weight gain
271 and reduced intake. This would mean that only 16 (8%), 67 (37%), and 26 (26%) in the UK,
272 Iran and Greece respectively, would be referred for further assessment; 75% of whom would
273 be true cases requiring dietetic input. However, this increase in positive predictive value
274 would be at cost of missing over a third of all children needing dietetic input (Table 3).

275 Previous studies have assessed the performance of nutritional screening tools against
276 the WHO criteria of acute and chronic malnutrition [7, 14]. However, the objective of a NST
277 is not just to identify sick children who are already malnourished, but also those likely to
278 become so in future, and it is these latter children who will make up the majority of cases
279 referred for dietetic input in most developed countries. Our benchmark does not represent an
280 absolute state of nutritional status, but instead reflects the characteristics of the children that
281 dietitians recognise as needing dietetic input. Only one other published screening tool has
282 also included infants, the STRONGkids tool, and we also tested its performance in the current
283 study. Compared with our benchmark of comprehensive dietetic assessment, STRONGkids
284 had a good positive predictive validity (63%) but lower sensitivity (41%) than iNEWS. From
285 the 66 children who had both measurements of BMI and skinfolds below the 2nd centile, 20
286 (30%) scored at high risk of malnutrition using STRONGkids, 43 (65%) scored moderate and
287 three (5%) rated as low risk. We made a similar observation in our European multicenter
288 study which compared all three popular screening tools [5] and this is possibly because health
289 professionals were required only to estimate body size by observation [15].

290 Most NST have been tested against weight-for-height or BMI, but this may be
291 misleading in chronically sick infants who commonly have low lean mass. Thus we explored
292 fat stores as an independent index of acute malnutrition. A limitation of this is the lack of
293 WHO reference data for skinfolds for infants aged under three months, which reduced the
294 available sample size. However high scoring infants, aged over 3 months, had much lower
295 levels of fatness and were more likely to have subnormal fat levels than their low scoring
296 counterparts. These differences were more striking in Greece and Iran. Some children with
297 low measurements of skinfolds did not have high iNEWS. These could be infants for whom
298 no ongoing nutritional concerns existed, despite low fatness levels, or infants whose low
299 fatness was masked by higher lean mass levels.

300 The main strengths of this study are the large sample size of infants in three different
301 countries, the objective statistical approach used to construct the iNEWS and decide its
302 threshold, the use of independent international cohorts for validation and the use of other
303 independent measures of nutritional risk to assess discriminant validity. A limitation is the
304 lack of comprehensive dietary assessment in the Iranian group. However, the equal
305 performance of iNEWS against skinfold measurements suggests that iNEWS would still
306 work well in this setting. iNEWS did not account for prematurity in assessing the weight
307 centile element, as this would have made the weight centile table and form (Figure 2) too
308 complex for nursing or junior medical staff to use. This may make ex-preterm infants more
309 likely to screen positive, but as this is a group at increased nutrition risk, this may be an
310 advantage rather than a limitation [16]. The use of convenience sampling, different referral
311 patterns to the different centres and the exclusion of children less than one month of age in
312 Iran, makes it almost certain that the type and severity of illness was different between the
313 centres, as well as the likely varying background risk of community malnutrition in these
314 countries. This can be considered a strength of the study though, as it tests the usefulness of
315 the tool in a range of health settings, but this means that these data cannot provide an estimate
316 of the true prevalence of undernutrition in hospitalised children in each country.

317 In conclusion, iNEWS appears to be an easy and valid tool to identify hospitalised
318 infants who need further dietetic input. Future research should evaluate its performance in
319 routine clinical practice and whether such screening improves overall clinical outcomes.

320

321 **Statement of authorship**

322 KG and CMW conceived and designed the study, KG, CMW, MR, MK co-ordinated and
323 supervised research activities in each centre; SM, AT, OP, CW, MT, AK, OZ, and KL
324 conducted the research; KG and SM performed statistical analysis; KG produced the first
325 draft manuscript; CMW and MK edited the first manuscript; all authors approved the final
326 submitted manuscript.

327

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329 conference attendance paid from Nestle, Mead Johnson, Nutricia and Dr Falk. The rest of the
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331

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340 **References**

341 [1] Huysentruyt K, Alliet P, Muyschont L, Devreker T, Bontems P, Vandenplas Y. Hospital-related
342 undernutrition in children: still an often unrecognized and undertreated problem. *Acta Paediatr.*
343 2013;102:e460-6.

344 [2] Agostoni C, Axelsson I, Colomb V, Goulet O, Koletzko B, Michaelsen KF, et al. The Need for
345 Nutrition Support Teams in Pediatric Units: A Commentary by the ESPGHAN Committee on Nutrition.
346 *Journal of Pediatric Gastroenterology and Nutrition.* 2005;41:8-11.

347 [3] Gerasimidis K, Keane O, Macleod I, Flynn DM, Wright CM. A four-stage evaluation of the
348 Paediatric Yorkhill Malnutrition Score in a tertiary paediatric hospital and a district general hospital.
349 *Br J Nutr.* 2010;104:751-6.

350 [4] Hulst JM, Zwart H, Hop WC, Joosten KF. Dutch national survey to test the STRONGkids nutritional
351 risk screening tool in hospitalized children. *Clin Nutr.* 2010;29:106-11.

352 [5] Chourdakis M, Hecht C, Gerasimidis K, Joosten KF, Karagiozoglou-Lampoudi T, Koetse HA, et al.
353 Malnutrition risk in hospitalized children: use of 3 screening tools in a large European population.
354 *The American journal of clinical nutrition.* 2016;103:1301-10.

355 [6] Huysentruyt K, Devreker T, Dejonckheere J, De Schepper J, Vandenplas Y, Cools F. Accuracy of
356 Nutritional Screening Tools in Assessing the Risk of Undernutrition in Hospitalized Children. *J Pediatr*
357 *Gastroenterol Nutr.* 2015;61:159-66.

358 [7] Moeeni V, Walls T, Day AS. Nutritional status and nutrition risk screening in hospitalized children
359 in New Zealand. *Acta Paediatr.* 2013;102:e419-23.

360 [8] Gerasimidis K, Macleod I, Maclean A, Buchanan E, McGrogan P, Swinbank I, et al. Performance of
361 the novel Paediatric Yorkhill Malnutrition Score (PYMS) in hospital practice. *Clin Nutr.* 2011;30:430-5.

362 [9] Hecht C, Weber M, Grote V, Daskalou E, Dell'Era L, Flynn D, et al. Disease associated malnutrition
363 correlates with length of hospital stay in children. *Clin Nutr.* 2015;34:53-9.

- 364 [10] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M, Educational, et al. ESPEN guidelines for
365 nutrition screening 2002. *Clin Nutr.* 2003;22:415-21.
- 366 [11] Huysentruyt K, Hulst J, Bian F, Shamir R, White M, Galera-Martinez R, et al. Opinions and
367 practices of healthcare professionals on assessment of disease associated malnutrition in children:
368 Results from an international survey. *Clin Nutr.* 2018.
- 369 [12] McCarthy H, Dixon M, Crabtree I, Eaton-Evans MJ, McNulty H. The development and evaluation
370 of the Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP(c)) for use by
371 healthcare staff. *J Hum Nutr Diet.* 2012;25:311-8.
- 372 [13] Cameron FL, Gerasimidis K, Papangelou A, Missiou D, Garrick V, Cardigan T, et al. Clinical
373 progress in the two years following a course of exclusive enteral nutrition in 109 paediatric patients
374 with Crohn's disease. *Aliment Pharmacol Ther.* 2013;37:622-9.
- 375 [14] Thomas PC, Marino LV, Williams SA, Beattie RM. Outcome of nutritional screening in the acute
376 paediatric setting. *Arch Dis Child.* 2016;101:1119-24.
- 377 [15] McKechnie J, Gerasimidis K. Visual inspection is not a substitute for anthropometry in screening
378 for nutritional status and growth in sick children. *Acta Paediatr.* 2015;104:e375-7.
- 379 [16] Olsen EM, Skovgaard AM, Weile B, Jorgensen T. Risk factors for failure to thrive in infancy
380 depend on the anthropometric definitions used: the Copenhagen County Child Cohort. *Paediatr*
381 *Perinat Epidemiol.* 2007;21:418-31.

382

383 **Figure Legends**

384

385 **Figure 1:** Participants flowchart

386 **Figure 2:** The infant nutrition early warning score

387 Panel A) numerical-based layout, Panel B) a decision-tree based algorithm

388 **Figure 3:** Concordance analysis between BMI Z-score and the mean of triceps and

389 subscapular Z-score

390

391 **Table Legends**

392 **Table 1:** Descriptive characteristics of the subjects in the three cohorts of the study

393 **Table 2:** Multivariate model including only significant predictors of outcome^a.

394 **Table 3:** Screening performance of iNEWS using alternative thresholds

395 **Table 4:** iNEWS screening performance compared with comprehensive dietetic assessment

396 and other anthropometric indices of nutritional risk.

Table 1: Descriptive characteristics of the subjects in the three cohorts of the study

	UK, N=210	Greece, N=102	Iran, N=187
<i>% (N)</i>			
Reason of admission			
<i>Medical infectious</i>	53% (111)	39% (40)	70% (131)
<i>Other medical</i>	23% (48)	36% (37)	14% (26)
<i>Surgical</i>	24% (51)	25% (25)	16% (30)
<i>Median, IQR</i>			
Age, years	0.32 (0.14 : 0.59)	0.40 (0.25 : 0.62)	0.33, (0.14 : 0.56)
Weight Z-score	-0.22 (-1.03 : 0.39)	-0.93 (-2.33 : -0.12)	-1.45 (-2.42 : -0.40)
Height Z-score	0.05 (-0.74 : 0.89)	0.23 (-1.13 : 1.25)	-0.41 (-1.70 : 0.54)
BMI Z-score	-0.30 (-1.22 : 0.34)	-1.60 (-2.52 : -0.75)	-1.52 (-2.54 : -0.71)
Average skinfolds Z-score	0.20 (-0.68 : 0.91)	-1.54 (-2.59 : -0.26)	-1.83 (-2.99 : -0.93)
MUAC Z-score	0.07 (-1.03 : 1.15)	-1.72 (-2.68 : -0.50)	-1.50 (-2.33 : -0.48)
<i>% (N)</i>			
Weight < 2 nd centile	12% (24)	32% (32)	35% (64)
Weight < 9 th centile	19% (39)	41% (41)	51% (94)
Height < 2 th centile	8% (15)	15% (15)	19% (34)
BMI < 2 th centile	12% (23)	36% (36)	39% (71)
Mean skinfolds < 9 th centile	12% (14)	58% (35)	65% (87)
Mean skinfolds < 2 th centile	6% (7)	43% (26)	44% (59)
MUAC < 11.5 cm	24% (50)	48% (47)	38% (70)

BMI: Body mass index; IQR: interquartile range; MUAC: Mid upper arm circumference; UK: United Kingdom

Table 2: Multivariate model including only significant predictors of outcome^a.

Predictors	β coefficient	Odd ratio (95% CI)	p-value
Weight			P<0.0001
2 nd centile	-3.99	0.019 (0.004, 0.087)	
9 th centile	-2.05	0.128 (0.016, 1.045)	
Poor weight gain/loss (yes)	-2.18	0.113 (0.028, 0.457)	P=0.002
Decrease in usual intake (yes)	-1.75	0.174 (0.042, 0.723)	P=0.012

^ai.e. valid request for dietetic input; CI: confidence intervals

Table 3: Screening performance of iNEWS using alternative thresholds

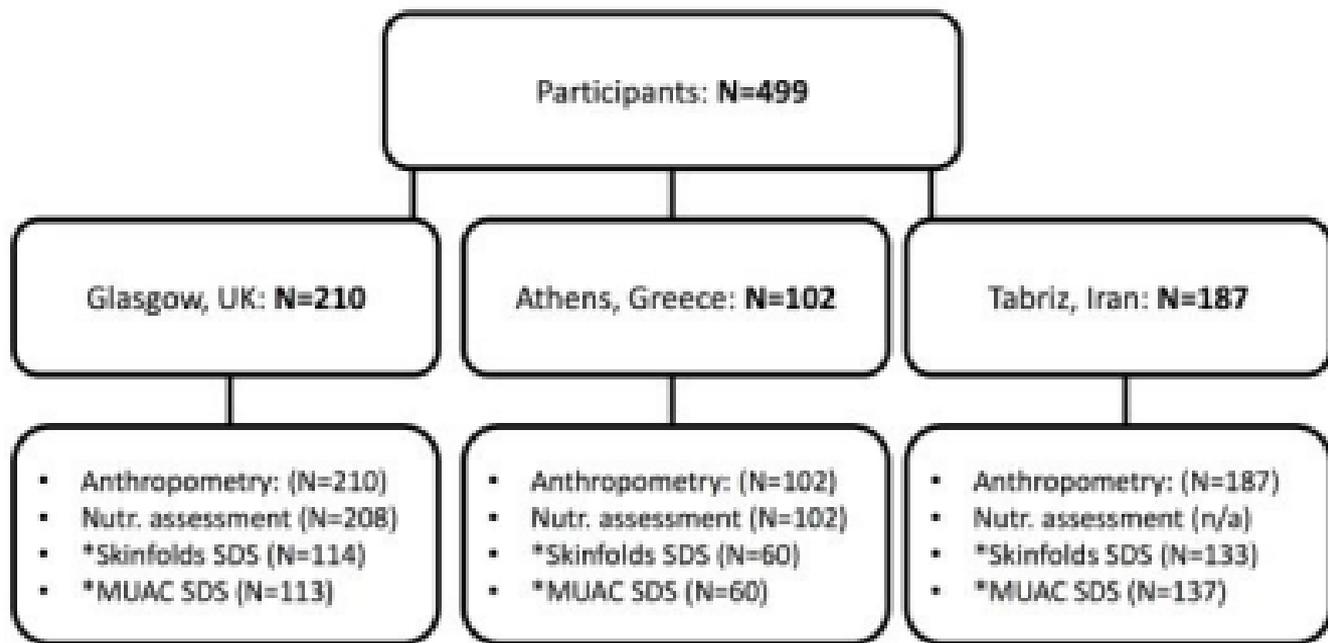
iNEWS threshold	Sensitivity (%)	95% CI	Specificity (%)	95% CI	PPV (%)	NPV (%)
1.7	94.7	74.0 - 99.9	56.8	49.3 - 64.1	18.8	99.0
2.0	89.5	66.9 - 98.7	78.1	71.4 - 83.9	30.3	98.6
2.2	89.5	66.9 - 98.7	84.1	78.0 - 89.1	37.4	98.9
3.8	84.2	60.4 - 96.6	90.2	84.9 - 94.1	47.7	98.2
3.9	84.2	60.4 - 96.6	90.7	85.5 - 94.5	49.0	98.2
4.0	78.9	54.4 - 93.9	93.4	88.8 - 96.6	55.9	97.7
4.2	63.2	38.4 - 83.7	97.8	94.5 - 99.4	75.3	96.2
5.7	57.9	33.5 - 79.7	98.4	95.3 - 99.7	79.3	95.6
5.9	42.1	20.3 - 66.5	98.9	96.1 - 99.9	80.2	94.1

CI: Confidence interval; NPV: Negative predictive value; PPV: Positive predictive value; Optimal cut-off is denoted with bold fonts

Table 4: iNEWS screening performance compared with comprehensive dietetic assessment and other anthropometric indices of nutritional risk.

	UK	Greece	Iran
Diagnostic values of iNEWS			
<i>Sensitivity</i>	84%	86%	NA
<i>Specificity</i>	91%	78%	NA
<i>Positive predictive value</i>	49%	53%	NA
<i>Negative predictive value</i>	98%	95%	NA
<i>Median, IQR</i>			
^a Average skinfold z-score			
<i>High iNEWS</i>	-0.81 (-1.83 : 0.24)	-2.60 (-3.10 : -1.21)	-2.81 (-3.53 : -1.96)
<i>Low iNEWS</i>	0.27 (-0.50 : 1.15)	-1.29 (-2.10 : -0.02)	-1.05 (-1.72 : -0.39)
<i>p-value</i>	0.004	0.001	<0.001
^a Median MUAC z-score			
<i>High iNEWS</i>	-1.73 (-2.63 : -1.11)	-2.54 (-3.63 : -1.89)	-2.29 (-3.38 : -1.64)
<i>Low iNEWS</i>	0.31 (-0.52 : 1.24)	-0.62 (-2.17 : 0.15)	-0.54 (-1.34 : 0.06)
<i>p-value</i>	<0.001	<0.001	<0.001
<i>% (N)</i>			
High iNEWS score	16% (33)	36% (36)	46% (83)
Average skinfold < 2 nd centile	6% (7)	43% (26)	45% (59)
<i>High iNEWS</i>	29% (2)	54% (14)	80% (47)
BMI < 2 nd centile	12% (23)	36% (36)	39% (70)
<i>High iNEWS</i>	18% (78)	72% (26)	84% (59)

^a for children > 3 months for whom WHO standards exist; BMI: Body mass index; MUAC: Mid upper arm circumference; NA: non-applicable



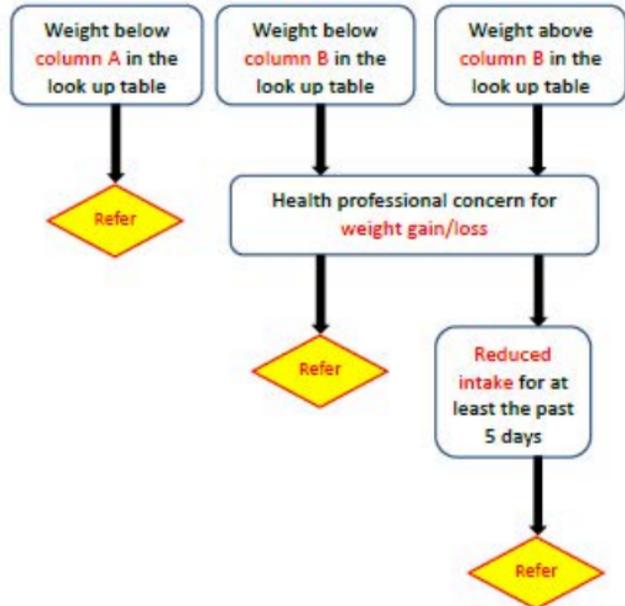
* N of patients with measurements and for whom WHO standards for calculation of Z-scores (SDS) were available
n/a: nutritional assessment was not available in Iran

Name:	Sex:	
DoB:	Weight (to nearest 10g):	Ward: _____
Date of screening:	Hospital number:	
		Score
STEP 1: Is a health professional concerned about your child's weight gain?	YES	2.2
STEP 2: Has your child had a reduced intake (including feeds) for at least the past 6 days ?	YES	1.7
STEP 3: Is the weight of the infant below column A or column B in the weight lookup table below?	YES, below column A	4
	YES, below column B	2

Age of infant in months	Weight lookup table for STEP 3			
	Columns for Males		Columns for Females	
	A	B	A	B
0	2.460	2.730	2.390	2.660
1	3.390	3.730	3.160	3.480
2	4.320	4.710	3.940	4.310
3	5.020	5.440	4.540	4.940
4	5.560	6.010	5.010	5.440
5	6.000	6.470	5.400	5.960
6	6.350	6.850	5.730	6.210
7	6.660	7.170	6.000	6.510
8	6.910	7.440	6.250	6.770
9	7.140	7.690	6.470	7.000
10	7.360	7.920	6.670	7.220
11	7.550	8.130	6.860	7.420

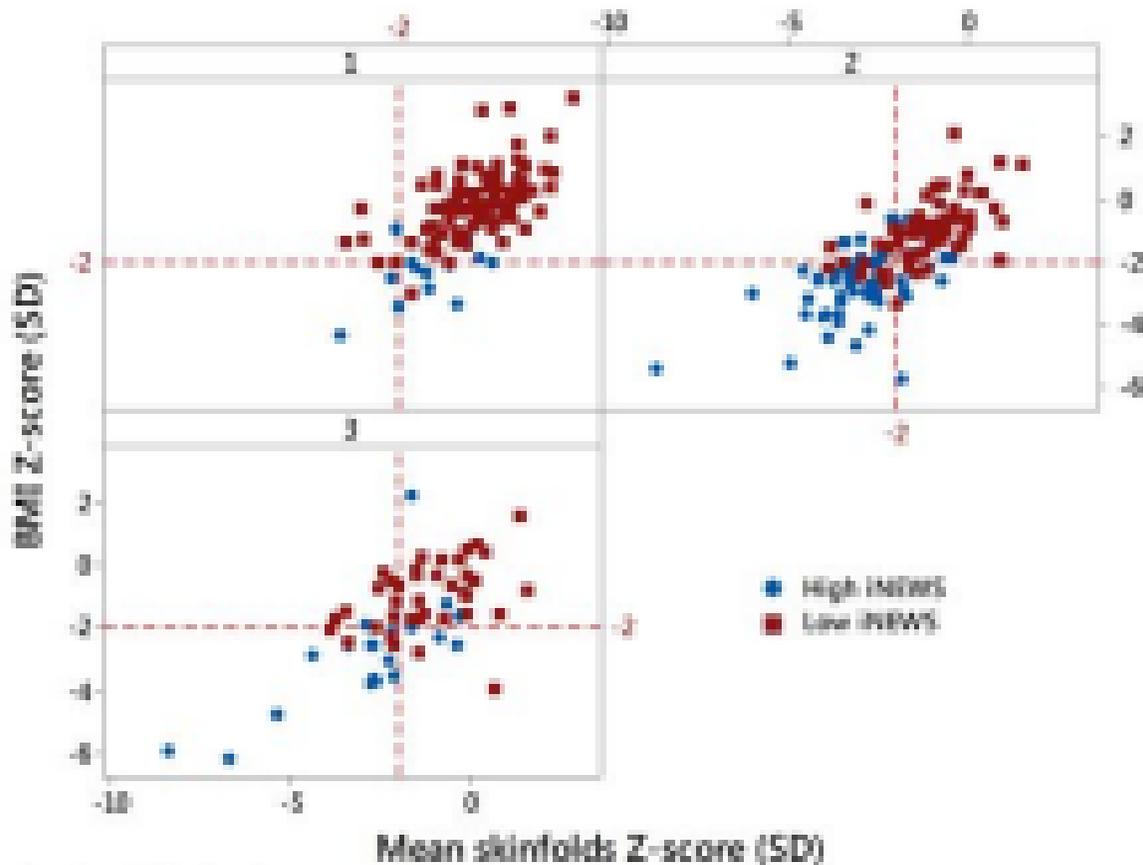
STEP 4: Add together the scores from STEPS 1, 2 and 3 and record the total score	Total iNEWS Score: _____
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Refer patient for further assessment if total iNEWS score is equal to or greater than 3.9



Age of infant in months	Weight lookup table			
	Columns for Males		Columns for Females	
	A	B	A	B
0	2.460	2.730	2.390	2.660
1	3.390	3.730	3.160	3.480
2	4.320	4.710	3.940	4.310
3	5.020	5.440	4.540	4.940
4	5.560	6.010	5.010	5.440
5	6.000	6.470	5.400	5.960
6	6.350	6.850	5.730	6.210
7	6.660	7.170	6.000	6.510
8	6.910	7.440	6.250	6.770
9	7.140	7.690	6.470	7.000
10	7.360	7.920	6.670	7.220
11	7.550	8.130	6.860	7.420

B)
A)



Panel variable: Country